

Amendments to the Claims

1.-9. (Canceled)

10. (currently amended) A method for treating female sexual arousal disorder comprising:

orally administering to a female subject in need thereof, an effective amount of an estrogen agonist / antagonist, and further comprising orally co-administering a cyclic guanosine 3',5'-monophosphate elevator.

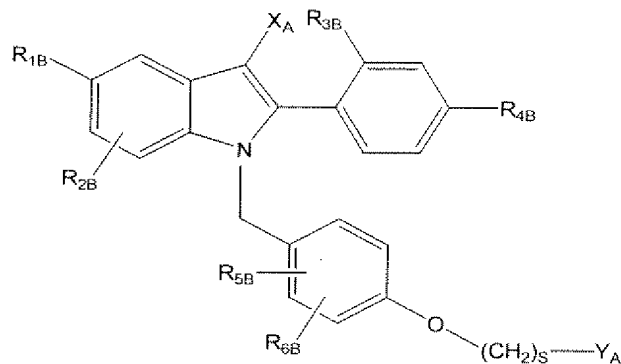
11. (previously presented) The method of claim 10 wherein said cyclic guanosine 3',5'-monophosphate elevator is a PDE<sub>V</sub> phosphodiesterase inhibitor.

12. (previously presented) The method of claim 11 wherein the PDE<sub>V</sub> phosphodiesterase inhibitor is 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxy-phenyl]sulfonyl]-4-methylpiperazine citrate salt.

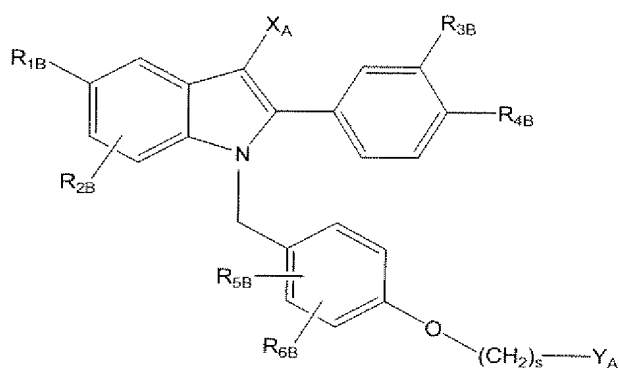
Claims 13.-39. (canceled)

40. (previously presented) The method of claim 10 wherein said estrogen agonist / antagonist is selected from the group consisting of tamoxifen, 4-hydroxy tamoxifen, raloxifene, toremifene, centchroman, idoxifene, 6-(4-hydroxy-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-benzyl]-naphthalen-2-ol, {4-[2-(2-aza-bicyclo[2.2.1]hept-2-yl)-ethoxy]-phenyl}-[6-hydroxy-2-(4-hydroxy-phenyl)-benzo[b]thiophen-3-yl]-methanone, EM-652, EM-800, GW 5638, GW 7604, or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or prodrug thereof.

41. (previously presented) The method of claim 10 wherein said estrogen agonist / antagonist is a compound selected from the formulas V or VI:



(V)



(VI)

wherein:

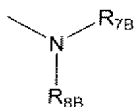
$R_{1B}$  is selected from H, OH,  $-O-C(O)-C_1-C_{12}$  alkyl (straight chain or branched),  $-O-C_1-C_{12}$  alkyl (straight chain or branched or cyclic), or halogens or  $C_1-C_4$  halogenated ethers,

$R_{2B}$ ,  $R_{3B}$ ,  $R_{4B}$ ,  $R_{5B}$ , and  $R_{6B}$  are independently selected from H, OH,  $-O-C(O)-C_1-C_{12}$  (straight chain or branched),  $-O-C_1-C_{12}$  (straight chain or branched or cyclic), halogens, or  $C_1-C_4$  halogenated ethers, cyano,  $C_1-C_6$  alkyl (straight chain or branched), or trifluoromethyl, with the proviso that, when  $R_{1B}$  is H,  $R_{2B}$  is not OH;

$X_A$  is selected from H,  $C_1-C_6$  alkyl, cyano, nitro, trifluoromethyl, and halogen;

s is 2 or 3;

$Y_A$  is the moiety:



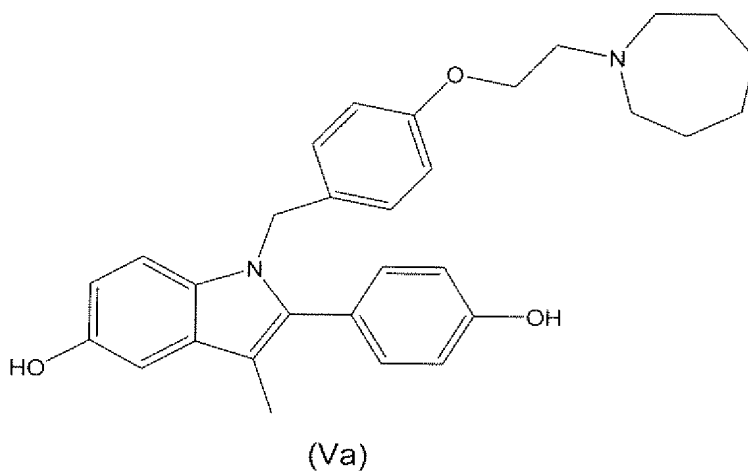
wherein:

- a)  $R_{7B}$  and  $R_{8B}$  are independently selected from the group of H,  $C_1$ - $C_6$  alkyl, or phenyl optionally substituted by CN,  $C_1$ - $C_6$  alkyl (straight chain or branched),  $C_1$ - $C_6$  alkoxy (straight chain or branched), halogen, -OH, - $CF_3$ , or - $OCF_3$ ; or
- b)  $R_{7B}$  and  $R_{8B}$  are concatenated to form a five-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo,  $C_1$ - $C_4$  alkyl, trihalomethyl,  $C_1$ - $C_4$  alkoxy, trihalomethoxy,  $C_1$ - $C_4$  acyloxy,  $C_1$ - $C_4$  alkylthio,  $C_1$ - $C_4$  alkylsulfinyl,  $C_1$ - $C_4$  alkylsulfonyl, hydroxy ( $C_1$ - $C_4$ )alkyl, - $CO_2H$ , -CN, - $CONHR_{1B}$ , - $NH_2$ , - $NH(C_1-C_4 \text{ alkyl})$ , - $N(C_1-C_4 \text{ alkyl})_2$ , - $NHSO_2R_{1B}$ , - $NHCOR_{1B}$ , - $NO_2$ , or phenyl optionally substituted with 1-3 ( $C_1$ - $C_4$ )alkyl; or
- c)  $R_{7B}$  and  $R_{8B}$  are concatenated to form a six-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo,  $C_1$ - $C_4$  alkyl, trihalomethyl,  $C_1$ - $C_4$  alkoxy, trihalomethoxy,  $C_1$ - $C_4$  acyloxy,  $C_1$ - $C_4$  alkylthio,  $C_1$ - $C_4$  alkylsulfinyl,  $C_1$ - $C_4$  alkylsulfonyl, hydroxy ( $C_1$ - $C_4$ )alkyl, - $CO_2H$ , -CN, - $CONHR_{1B}$ , - $NH_2$ , - $NH(C_1-C_4 \text{ alkyl})$ , - $N(C_1-C_4 \text{ alkyl})_2$ , - $NHSO_2R_{1B}$ , - $NHCOR_{1B}$ , - $NO_2$ , or phenyl optionally substituted with 1-3 ( $C_1$ - $C_4$ )alkyl; or
- d)  $R_{7B}$  and  $R_{8B}$  are concatenated to form a seven-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo,  $C_1$ - $C_4$  alkyl, trihalomethyl,  $C_1$ - $C_4$  alkoxy, trihalomethoxy,  $C_1$ - $C_4$  acyloxy,  $C_1$ - $C_4$  alkylthio,  $C_1$ - $C_4$  alkylsulfinyl,  $C_1$ - $C_4$  alkylsulfonyl, hydroxy ( $C_1$ - $C_4$ )alkyl, - $CO_2H$ , -CN, - $CONHR_{1B}$ , - $NH_2$ , - $NH(C_1-C_4 \text{ alkyl})$ , - $N(C_1-C_4 \text{ alkyl})_2$ , - $NHSO_2R_{1B}$ , - $NHCOR_{1B}$ , - $NO_2$ , or phenyl optionally substituted with 1-3 ( $C_1$ - $C_4$ )alkyl; or

e)  $R_{7B}$  and  $R_{8B}$  are concatenated to form an eight-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo,  $C_1$ - $C_4$  alkyl, trihalomethyl,  $C_1$ - $C_4$  alkoxy, trihalomethoxy,  $C_1$ - $C_4$  acyloxy,  $C_1$ - $C_4$  alkylthio,  $C_1$ - $C_4$  alkylsulfinyl,  $C_1$ - $C_4$  alkylsulfonyl, hydroxy ( $C_1$ - $C_4$ )alkyl,  $-CO_2H$ ,  $-CN$ ,  $-CONHR_1$ ,  $-NH_2$ ,  $-NH(C_1-C_4 \text{ alkyl})$ ,  $-N(C_1-C_4 \text{ alkyl})_2$ ,  $-NHSO_2R_{1B}$ ,  $-NHCOR_{1B}$ ,  $-NO_2$ , or phenyl optionally substituted with 1-3 ( $C_1$ - $C_4$ )alkyl; or

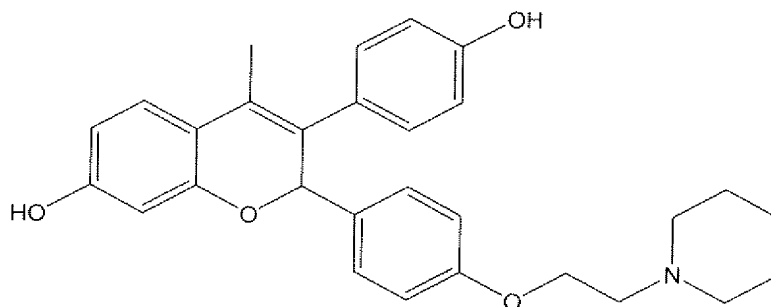
f)  $R_{7B}$  and  $R_{8B}$  are concatenated to form a saturated bicyclic heterocycle containing from 6-12 carbon atoms either bridged or fused and containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo,  $C_1$ - $C_4$  alkyl, trihalomethyl,  $C_1$ - $C_4$  alkoxy, trihalomethoxy,  $C_1$ - $C_4$  acyloxy,  $C_1$ - $C_4$  alkylthio,  $C_1$ - $C_4$  alkylsulfinyl,  $C_1$ - $C_4$  alkylsulfonyl, hydroxy ( $C_1$ - $C_4$ )alkyl,  $-CO_2H$ ,  $-CN$ ,  $-CONHR_{1B}$ ,  $-NH_2$ ,  $-NH(C_1-C_4 \text{ alkyl})$ ,  $-N(C_1-C_4 \text{ alkyl})_2$ ,  $-NHSO_2R_{1B}$ ,  $-NHCOR_{1B}$ ,  $-NO_2$ , or phenyl optionally substituted with 1-3 ( $C_1$ - $C_4$ ) alkyl; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

42. (previously presented) The method of claim 41 wherein said estrogen agonist / antagonist is the compound, TSE-424, of formula Va below:

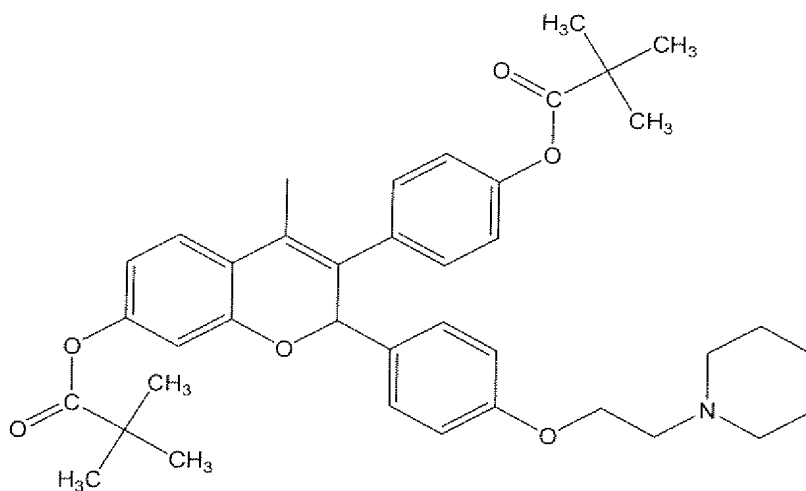


or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

43. (previously presented) The method of claim 10 wherein said estrogen agonist / antagonist is EM-652 of formula III below or is EM-800 of formula IV below:



(III)



(IV)

or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

44. – 45. (Canceled)

46. (currently amended) A method for treating female sexual arousal disorder comprising:

orally administering to a female subject in need thereof, an effective amount of (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof and further comprising orally co-administering an effective amount of a cyclic guanosine 3',5'-monophosphate elevator.

47. (previously presented) The method of claim 46 wherein the cyclic guanosine 3',5'-monophosphate elevator is a PDE<sub>V</sub> phosphodiesterase inhibitor.

48. (previously presented) The method of claim 47 wherein the PDE<sub>V</sub> phosphodiesterase inhibitor is 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxy-phenyl]sulfonyl]-4-methylpiperazine citrate salt.

49. (canceled)

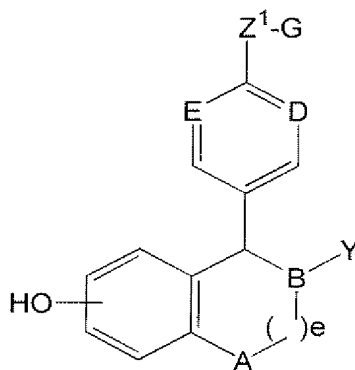
50. (previously presented) The method of claim 46, 47 or 48 wherein (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol, D-tartrate salt is administered.

51. (previously presented) The method of claim 48 wherein the female subject is premenopausal.

52. (previously presented) The method of claim 46 wherein the female subject is postmenopausal.

53. (previously presented) The method of claim 46 wherein the female subject is premenopausal.

54. (previously presented) The method of claim 10 wherein the estrogen agonist/antagonist is a compound of formula (I):



(I)

wherein:

A is selected from  $\text{CH}_2$  and  $\text{NR}$ ;

B, D and E are independently selected from CH and N;

Y is

(a) phenyl, optionally substituted with 1-3 substituents independently selected from  $\text{R}^4$ ;

(b) naphthyl, optionally substituted with 1-3 substituents independently selected from  $\text{R}^4$ ;

(c)  $\text{C}_3$ - $\text{C}_8$  cycloalkyl, optionally substituted with 1-2 substituents independently selected from  $\text{R}^4$ ;

(d)  $\text{C}_3$ - $\text{C}_8$  cycloalkenyl, optionally substituted with 1-2 substituents independently selected from  $\text{R}^4$ ;

(e) a five membered heterocycle containing up to two heteroatoms selected from the group consisting of  $-\text{O}-$ ,  $-\text{NR}^2-$  and  $-\text{S}(\text{O})_n-$ , optionally substituted with 1-3 substituents independently selected from  $\text{R}^4$ ;

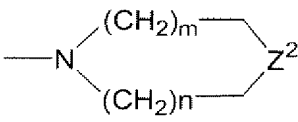
(f) a six membered heterocycle containing up to two heteroatoms selected from the group consisting of  $-\text{O}-$ ,  $-\text{NR}^2-$  and  $-\text{S}(\text{O})_n-$  optionally substituted with 1-3 substituents independently selected from  $\text{R}^4$ ; or

(g) a bicyclic ring system consisting of a five or six membered heterocyclic ring fused to a phenyl ring, said heterocyclic ring containing up to two heteroatoms selected from the group consisting of  $-\text{O}-$ ,  $-\text{NR}^2-$  and  $-\text{S}(\text{O})_n-$ , optionally substituted with 1-3 substituents independently selected from  $\text{R}^4$ ;

$\text{Z}^1$  is

- (a)  $-(\text{CH}_2)_p \text{W}(\text{CH}_2)_q-$ ;
- (b)  $-\text{O}(\text{CH}_2)_p \text{CR}^5\text{R}^6-$ ;
- (c)  $-\text{O}(\text{CH}_2)_p \text{W}(\text{CH}_2)_q-$ ;
- (d)  $-\text{OCHR}^2\text{CHR}^3-$ ; or
- (e)  $-\text{SCHR}^2\text{CHR}^3-$ ;

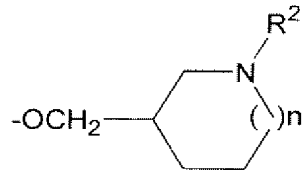
G is

- (a)  $-\text{NR}^7\text{R}^8$ ;
- (b) 

wherein n is 0, 1 or 2; m is 1, 2 or 3;  $\text{Z}^2$  is  $-\text{NH}-$ ,  $-\text{O}-$ ,  $-\text{S}-$ , or  $-\text{CH}_2-$ ;

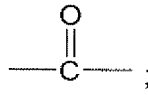
optionally fused on adjacent carbon atoms with one or two phenyl rings and, optionally independently substituted on carbon with one to three substituents and, optionally, independently on nitrogen with a chemically suitable substituent selected from  $\text{R}^4$ ; or

(c) a bicyclic amine containing five to twelve carbon atoms, either bridged or fused and optionally substituted with 1-3 substituents independently selected from  $\text{R}^4$ ; or

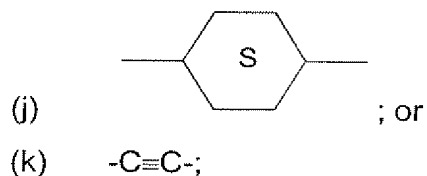


$\text{Z}^1$  and G in combination may be

W is

- (a)  $-\text{CH}_2-$ ;
- (b)  $-\text{CH}=\text{CH}-$ ;
- (c)  $-\text{O}-$ ;
- (d)  $-\text{NR}^2-$ ;
- (e)  $-\text{S}(\text{O})_n-$ ;
- (f) ;
- (g)  $-\text{CR}^2(\text{OH})-$ ;
- (h)  $-\text{CONR}^2-$ ;
- (i)  $-\text{NR}^2\text{CO}-$ ;





R is hydrogen or  $\text{C}_1\text{-C}_6$  alkyl;

$\text{R}^2$  and  $\text{R}^3$  are independently

- (a) hydrogen; or
- (b)  $\text{C}_1\text{-C}_4$  alkyl;

$\text{R}^4$  is

- (a) hydrogen;
- (b) halogen;
- (c)  $\text{C}_1\text{-C}_6$  alkyl;
- (d)  $\text{C}_1\text{-C}_4$  alkoxy;
- (e)  $\text{C}_1\text{-C}_4$  acyloxy;
- (f)  $\text{C}_1\text{-C}_4$  alkylthio;
- (g)  $\text{C}_1\text{-C}_4$  alkylsulfinyl;
- (h)  $\text{C}_1\text{-C}_4$  alkylsulfonyl;
- (i) hydroxy ( $\text{C}_1\text{-C}_4$ )alkyl;
- (j) aryl ( $\text{C}_1\text{-C}_4$ )alkyl;
- (k)  $\text{-CO}_2\text{H}$ ;
- (l)  $\text{-CN}$ ;
- (m)  $\text{-CONHOR}$ ;
- (n)  $\text{-SO}_2\text{NHR}$ ;
- (o)  $\text{-NH}_2$ ;
- (p)  $\text{C}_1\text{-C}_4$  alkylamino;
- (q)  $\text{C}_1\text{-C}_4$  dialkylamino;
- (r)  $\text{-NHSO}_2\text{R}$ ;
- (s)  $\text{-NO}_2$ ;
- (t)  $\text{-aryl}$ ; or
- (u)  $\text{-OH}$ ;

$\text{R}^5$  and  $\text{R}^6$  are independently  $\text{C}_1\text{-C}_8$  alkyl or together form a  $\text{C}_3\text{-C}_{10}$  carbocyclic ring;

$R^7$  and  $R^8$  are independently

- (a) phenyl;
- (b) a  $C_3$ - $C_{10}$  carbocyclic ring, saturated or unsaturated;
- (c) a  $C_3$ - $C_{10}$  heterocyclic ring containing up to two heteroatoms, selected from -O-, -N- and -S-;
- (d) H;
- (e)  $C_1$ - $C_6$  alkyl; or
- (f) form a 3 to 8 membered nitrogen containing ring with  $R^5$  or  $R^6$ ;

$R^7$  and  $R^8$  in either linear or ring form may optionally be substituted with up to three substituents independently selected from  $C_1$ - $C_6$  alkyl, halogen, alkoxy, hydroxy and carboxy;

a ring formed by  $R^7$  and  $R^8$  may be optionally fused to a phenyl ring;

e is 0, 1 or 2;

m is 1, 2 or 3;

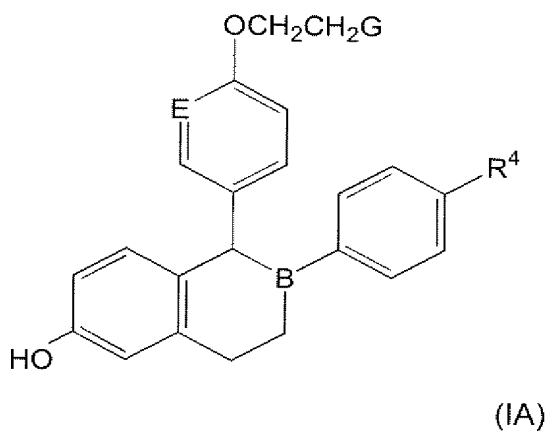
n is 0, 1 or 2;

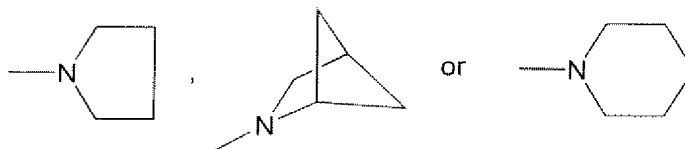
p is 0, 1, 2 or 3;

q is 0, 1, 2 or 3;

or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

55. (previously presented) The method of claim 54 wherein said estrogen agonist / antagonist is a compound of formula (IA):





wherein G is

;

$R^4$  is H, OH, F, or Cl; and B and E are independently selected from CH and N or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof.